

REMARKS

Applicants would thank Examiners Lankford and Schuberg for their participation in a telephonic interview, conducted on February 28, 2008, which also involved applicants' U.S. counsel, their European counsel, and Dr. Laurent Meijer, a co-inventor. Applicants request reconsideration of this application in view of the foregoing revisions and these remarks.

I. Status of the Claims

Claim 1 has been amended to characterize the recited inhibitor as targeting "CDK/cyclin kinase" and to qualify the treated "deafness" condition as occasioned by the "death of sensory hair cells." These changes comport with those discussed during the February 28th interview, when the examiners were heard to express an acceptance, in principle, of the amendments and applicants' view of their significance, as elaborated below.

The present amendments introduce no new matter, finding ample support in the original specification, e.g., between paragraphs 0003 and 0016 of the published version. Entry of these revisions is requested, whereupon claims 1, 3 – 9, and 11 – 14 will be pending.

II. Rejection Under 35 U.S.C. § 103

All of the claims stand rejected for obviousness over the combination of Meijer (WO 01/41768) with Santora *et al.* (US 2002/0173507) and Nicotera *et al.* (US 2004/0019015). The essence of the rationale for rejection is understood to be that

...one of ordinary skill ... would have been motivated to use the method of Meijer to treat hearing loss caused by nerve damage because Santora *et al.* teach that neurodegenerative disorders include hearing loss ... and can be treated with a CDK/cyclin kinase inhibitor. ... One of ordinary skill ... would have had a reasonable expectation of success [in this effort] because Nicotera *et al.* teach using protein kinase inhibitors to treat hearing loss in the same formats as Meijer and at the same dosage.

Action at page 5, line 16, to page 6, line 5 (citations omitted).

As was discussed during the interview, however, one linchpin of this rationale, the passing reference by the Santora reference to “hearing loss” in a veritable laundry list of “neurological disorders” (paragraph 0361), is linked to an express teaching that the disclosed “compounds ... are useful to prevent the phosphorylation of tau protein.” The latter is a substrate having an involvement in Alzheimer’s and certain other neurodegenerative diseases (see Meijer at page 3, lines 11 – 19) but no known connection to hearing loss, as Dr. Meijer confirmed during the interview.

Accordingly, one of ordinary skill would have had no principled motivation for adapting “the method of Meijer” to the treatment of a particular type of deafness, as presently recited, by means of a physiological effect – inducing differentiation of the prescribed sensory cells to replace cells lost to cell death – that embodied *applicants’* discovery, not the art’s, and that bears no known relationship to tau phosphorylation. Furthermore, Nicotera *et al.* would have prompted no reasonable expectation of success in the context, contrary to the aforementioned rationale. The Nicotera reference relates to a different class of compounds (“PKT inhibitors”) and to a different physiological effect, “prevent[ing] apoptosis of cochlear hair cells” (paragraph 0078; emphasis added), which would be of no avail for a subject whose deafness arose from extant cell death, as presently recited.

In light of the foregoing, therefore, applicants submit the respective teachings of Meijer, Nicotera *et al.*, and Santora *et al.*, even were they combinable in the manner posited in the Office Action, would not have led the skilled artisan to the presently claimed invention. Reconsideration and withdrawal of the pending obviousness rejection are warranted, therefore.

CONCLUSION

Applicants further submit that the application is in condition for allowance, and they request an early indication to this effect. Examiner Schuberg is invited to contact the undersigned directly, should she feel that any issue requires further consideration.

The Commissioner is hereby authorized to charge any additional fees, which may be required under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the

unpaid amount to the same deposit account. If any extension is needed for timely acceptance of submitted papers, Applicants hereby petition for such extension under 37 CFR §1.136 and authorizes payment of any such extensions fees from the deposit account.

Respectfully submitted,

Date 1 March 2008

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